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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
FORD, VANESSA L	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 08/30/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/677,752	JACKSON, W. JAMES	
	Examiner	Art Unit	
	Vanessa L. Ford	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 May 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *94,95 and 99-129* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *94,95,99-103,105 and 106* is/are allowed.

6)☒ Claim(s) *104 and 107-129* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 December 2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/25/04&6/7/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on May 25, 2004 has been entered.

Specification Objection

2. This application also fails to comply the requirements of 37 C.F.R. 1.821-1.825 because it contains sequences that are not identified. For example, in the drawing, for example, (figures 5A-E and figure 6A-E) contain sequences that are not identified. Appropriate sequence identifiers should be used to comply with sequence rules. The sequences in the specification and drawings should match the sequence listing and computer readable form (CRF) submitted with the application. Applicant is required to review the specification for unidentified sequences and the identification of these sequences is required.

Claim Objection

3. Claim 125 is objected to for the following informality: "*Nisseria*" should be changed to "*Neisseria*". Correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 107-129 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for SEQ ID NO:2, does not reasonably provide enablement for amino acids that are at least 90% identical to SEQ ID NO:2 (which include variants, homologs, degenerates, derivatives of SEQ ID NO:2) or fragments of SEQ ID NO:2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification is enabling only for the polynucleotide of SEQ ID NO: 2 and not variants (polypeptides that are at least 90% identical to SEQ ID No:2) of SEQ ID NO:2. The specification discloses SEQ ID NO: 2 which correspond to the amino acid sequence that encodes a PMPE polypeptide. The claims are directed to sequences that are substantially homologous to SEQ ID NO: 2 which encompassed corresponding sequences from other species, mutated sequences, allelic variants, splice variants, sequences that have a variant degree of identity (similarity, homology), and so forth. There is no guidance provided as to which amino acids can be added, deleted or substituted and still have the polypeptide retain its biological function. Thus, the

resulting polypeptide could result in a polypeptide not taught nor enabled by the specification.

Thomas E. Creighton, in his book, "*Proteins: Structures and Molecular Properties, 1984",* (pages 314-315) teaches that variation of the primary structure of a protein can result in an instable molecule. He teaches that a single amino acid change can cause a mutant hemoglobin to have lower stabilities due to any of several causes: 1) alteration of close-packing of the interior; loss of one group that normally participates in a hydrogen bond or salt bridge; 2) the introduction of a charged or polar group into the interior or the insertion into a helical region of a Praline residue, which must distort the alpha-helix; 3) while sometimes radical changes of surface groups, even introduction of a non-polar side chain- have no great effect on stability.

Thomas E. Creighton, in his book "*Protein Structure: A Practical Approach, 1989; pages 184-186"* teaches that present day site directed mutagenesis of a gene allows any amino acids in a protein sequence to be changed to any other, as well as introducing deletions and insertions". The reference goes on to teach that it is difficult to know which amino acid to change and which is the best residue to substitute for the desired functional and structural effect.

Nosoh, Y. et al in "*Protein Stability and Stabilization through Protein Engineering, 1991" (chapter 7, page 197, second paragraph)* adds support to Thomas E. Creighton, by teaching that results so far accumulated on the stability and stabilization of proteins appear to indicate that the strategy for stabilizing proteins differ from protein to protein and that any generalized mechanisms for protein stability have not yet been presented.

The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polypeptides broadly encompassed by the claims and the claims broadly encompass a significant number of inoperative species. Since the amino acid sequence of the polypeptide determines its structural and functional properties, predictability of which changes can be tolerated in an amino acid's sequence and still retain similar activity requires a knowledge with regard to which amino acids in the polypeptide's sequence, if any, are tolerant of modification and which are conserved (i.e. expected intolerant to modification) and detailed knowledge of the ways in which the polypeptide's structure relates to function. However, the problem of the prediction of polypeptide's structure from mere sequence data of a single polypeptide and in turn utilizing predicted structural determinations to ascertain functional aspects of the polynucleotide and finally what changes can be tolerated with respect thereto is extremely complex and outside of the realm of routine experimentation.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen multiple substitutions or multiple modifications of other types and the positions within the polypeptide's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining similar activity are limited in any polynucleotide and the result of such modifications is unpredictable based on the instant disclosure. One skilled in the art would expect any tolerance to modifications, e.g., multiple substitutions. The sequence of some polynucleotide is highly conserved

and one skilled in the art would not expect tolerance to any amino acid modification in such polypeptides.

The claims of the instant application are not only drawn to a purified nucleic acid molecule but are also drawn to fragments of the polypeptide, which comprises at least 8 amino acids. There is no guidance provided in the specification as how one would begin to choose "at least 8 amino acids". The specification does not support the broad scope of the claims, which encompass all modifications and fragments because the specification does not disclose the following:

- the general tolerance to modification and extent of such tolerance;
- specific positions and regions of sequence(s) which can be predictably modified and which regions are critical;
- what fragments, if any, can be made which the retain the biological activity if the intact polypeptide; and
- the specification provides essentially no guidance as to which of the essentially infinite possible choice is likely to be successful.

Factors to be considered in determining whether undue experimentation is required, are set forth in In re Wands 8 USPQ2d 1400. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims.

Applying the above test to the facts of record, it is determined that 1) no declaration under 37 C.F.R. 1.132 or other relevant evidence has been made of record establishing the amount of experimentation necessary, 2) insufficient direction or guidance is presented in the specification with respect to selecting other polypeptides having claimed functional features, 3) the relative skill of those in the art is commonly recognized as quite high (post-doctoral level). One of skill in the art would require guidance, in order to make or use polypeptide that are variants, homologs, degenerates, derivatives or fragments of SEQ ID NO: 7 in a manner reasonable in correlation with the scope of the claims. Without proper guidance, the experimentation to is undue.

The Applicant has not provided sufficient guidance to enable one of skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of additions, deletions or substitutions and fragments of any size. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970). Without such guidance, the changes which can be made in the polypeptide's structure and still maintain activity is unpredictable and the experimentation left those skilled in the art is unnecessarily and improperly, extensive and undue. See Amgen Inc v Chugai Pharmaceutical Co Ltd. 927 F 2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991) at 18 USPQ2d 1026-1027 and Exparte Forman, 230 U.S. P.Q. 546(Bd. Pat=. App & int. 1986).

In view of all of the above, in view of the lack of predictability in the art, it is determined that it would require undue experimentation to make and use the claimed invention commensurate in scope with the claims.

5. Claims 104 and 125 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for vaccine compositions that comprise an isolated putative membrane protein E (PMPE) does not reasonably provide enablement for vaccine compositions that comprise an isolated putative membrane protein E (PMPE) and immunogens such as HIV *and Moraxella catarrhalis*. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification teaches that the compositions of the claimed invention can be used to provide therapeutic and prophylactic treatment and prevention of *Chlamydia* infections (page 43). The specification teaches that the compositions of the invention include vaccine compositions (page 43). The specification teaches that the compositions of the claimed invention can be formulated into combination compositions that include other immunogens such as HIV and *Moraxella catarrhalis* (page 43). The term "vaccine" encompasses the ability of the specific antigen to induce protective immunity to infection or disease induction.

The specification has failed to teach or disclose how the claimed compositions can be used to prevent for example, infections caused by HIV and *Moraxella catarrhalis*. The state of the art regarding HIV and *Moraxella catarrhalis* vaccines is cited below:

It is well known in the art that there are several different antigens from *Moraxella catarrhalis* (i.e. outer membrane proteins and lipooligosaccharides). It is also taught that since infections caused by *Moraxella* predominately occur on mucosal surfaces, the mucosal immune response is likely important as the first line of defense. Mucosal or surface antigen immune response would likely be important in the search for candidate vaccines Kyd et al, *(Vaccine 18 (2000), 398-406)).* It has also been recognized in the art that there is currently no vaccine to prevent *Moraxella catarrhalis* infections because of a lack of good animal models for the diseases, a lack of information about the protective antigens, a lack of *in vitro* correlates to immunity against *Moraxella catarrhalis* in humans and the pathogenic mechanisms and host immune response to the pathogens has yet to be clarified (Samukawa et al, *(The Journal of Infectious Diseases, 2000, 181:1842-5)* and Kyd et al, *(Vaccine 18 (2000), 398-406)*). While studies have been shown that the outer membrane proteins can elicit bacterial antibodies, which promote bacterial clearance, the results have not lead to a predictable vaccine against infections caused by *Moraxella catarrhalis*. A similar situation exists with the development of lipooligosaccharides (LOS) based vaccines against infections caused by *Moraxella catarrhalis* (Gu et al, *Infection and Immunity, May 1998, p. 1891-1897).*

Fox (*Biotechnology, Vol. 12, February 1994)* teaches that the quest to develop both preventive and therapeutic HIV vaccines is proving a frustrating enterprise. Fox teaches that there are many themes regarding how to approach developing therapeutic agents against HIV infection. Fox teaches that these themes include the use of cytotoxic T lymphocytes, the use of envelope proteins as vaccines and the use of cytokines to

boost the immune system. Fox teaches that despite positive results regarding HIV and AIDS research, no therapy has emerged as a sure winner in the campaign against HIV, not a preventive vaccine nor therapeutic vaccine nor any of the immune-system-boosting treatments. Therefore, the prior art has taught that no "HIV protective epitopes" exist.

The cited prior art references indicate that it would require undue experimentation to formulate and use a successful vaccine against *Moraxella catarrhalis* or HIV infections without the prior demonstration of vaccine efficacy. The prior art cited has established that problems and barriers exist in vaccine development. The claimed invention broadly encompasses infection or disease caused by *Moraxella catarrhalis* or HIV. The specification has not shown a correlation between the claimed vaccine and *Moraxella catarrhalis* or HIV infections. The specification has not provided enablement for the claimed vaccines including immunogens from HIV and *Moraxella catarrhalis* since there are no working examples in the instant specification that demonstrate effectiveness of the polypeptide against these infections. One skilled in the art would have to possess the knowledge or be provided with sufficient guidance to determine if the vaccine compositions would reach the target microorganisms in order to treat or prevent infection. It would require undue experimentation by one of skill in the art to determine whether the claimed vaccine compositions would be effective in preventing *Moraxella catarrhalis* or HIV infections.

Factors to be considered in determining whether undue experimentation is required, are set forth in In re Wands 8 USPQ2d 1400. They include (1) the quantity of

experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims.

Applying the above test to the facts of record, it is determined that 1) no declaration under 37 C.F.R. 1.132 or other relevant evidence has been made of record establishing the amount of experimentation necessary, 2) insufficient direction or guidance is presented in the specification with respect to developing a vaccine composition that would achieve a desire level of success when administered to a patient to prevent, for example HIV and *Moraxella catarrhalis* infections or diseases, 3) there are no working examples which suggest the desired results of a successful vaccine composition that is to prevent HIV and *Moraxella catarrhalis* infections and 4) the relative skill of those in the art is commonly recognized as quite high (post - doctoral level).

In view of all of the above, it is determined that the specification has not provided guidance that would enable one of skill in the art to be able to make and use the claimed invention commensurate in scope with the claims. One of skill in the art would require undue experimentation to determine whether the claimed vaccine compositions could be used to prevent, for example HIV and *Moraxella catarrhalis* infections because the cited art teaches that no vaccines exists for HIV and *Moraxella catarrhalis* infections.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

6. Claims 107-122, 124 and 128-129 are rejected under 35 U.S.C. 102(b) as anticipated by Graffais et al *(WO 9928475, published June 10, 1999).*

Claims 107-122, 124 and 128-129 are drawn to a vaccine comprising an isolated recombinant putative membrane protein E (PMPE) polypeptide of a *Chlamydia* spp. comprising an amino acid sequence at least 90% identical to SEQ ID NO: 2 when % identity is determined using XBLAST program, score+50, word=3.

Griffais et al teach polypeptides from *Chlamydia trachomatis* that can be used in vaccines for the prevention and or treatment of *Chlamydia trachomatis* infections (see the Abstract). Griffais et al teach that vaccines of the invention contain a pharmaceutically acceptable vehicle and may contain adjuvants (page 76). Griffais et al teach a polypeptide (SEQ ID NO: 31) that is 99.2% identical to the claimed polypeptide

disclosed in SEQ ID NO:2. Therefore the polypeptide of the prior art, can specifically bind to an antibody that specifically binds to a protein comprising the amino acid of SEQ ID NO:2. Griffais et al teach that proteins and nucleic acid sequences were evaluated using BLAST (pages 9-10). See enclosed sequence alignment.

Although the reference appears to disclose vaccines comprising the same purified polypeptides claimed by the applicant's, the reference does not disclose that the purified polypeptides produced by the same claimed process. However, the purification or production of protein by a particular process does not impart novelty or unobviousness to a protein when the same protein is taught by the prior art. This is particularly true when the properties of the protein are not changed by the process in an unexpected manner. See In re Thorpe, 227 USPQ 964 (CAFC 1985); In re Marsosi, 218 USPQ 289, 292-293 (CAFC 1983); In re Brown, 173 USPQ 685 (CCPA 1972).

Since the Office does not have the facilities for examining and comparing applicant's vaccine and peptide fragment with the vaccine and peptide fragment of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the vaccine and peptide fragment of the prior art does not possess the same material structural and functional characteristics of the claimed vaccine and peptide fragment). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

7. Claims 107-122, 124 and 128-129 are rejected under 35 U.S.C. 102(a) as .anticipated by Probst et al *(WO 00/34483, published June 15, 2000).*

Claims 107-122, 124 and 128-129 are drawn to a vaccine comprising an isolated recombinant putative membrane protein E (PMPE) polypeptide of a *Chlamydia* spp. comprising an amino acid sequence at least 90% identical to SEQ ID NO: 2 when % identity is determined using XBLAST program, score+50, word=3.

Probst et al teach pharmaceutical compositions and vaccines comprising Chlamydial polypeptides (see the Abstract). Probst et al teach vaccines comprising antibodies (page 58 and page102, claim 22). Probst et al teach that the vaccines of the invention may comprise one or more polypeptide and an immunostimulant (pages 45-46). Probst et al teach that any variety of immunostimulants may be employed in the vaccine compositions of the invention and an adjuvant may be included (page 47). Probst et al teach that the vaccine may include a combination of adjuvants such as monophosphoryl lipid A (MPL) and saponin (QS21) (pages 48-49). Probst et al teach that any vaccine provided in the invention may include a combination of antigen, immune response enhancer and a suitable carrier or excipient (page 49). Probst et al teach SEQ ID NO:177 which is the predicted full-length amino acid sequence for *C. trachomatis* (page 17). Probst et al teach a polypeptide (SEQ ID NO: 177) that is 98% identical to SEQ ID NO:2 and comprises the claimed peptide fragment of SEQ ID NO: 5. See enclosed sequence alignment.

Although the reference appears to disclose vaccines comprising the same purified polypeptides claimed by the applicant's, the reference does not disclose that the

purified polypeptides produced by the same claimed process. However, the purification or production of protein by a particular process does not impart novelty or unobviousness to a protein when the same protein is taught by the prior art. This is particularly true when the properties of the protein are not changed by the process in an unexpected manner. See In re Thorpe, 227 USPQ 964 (CAFC 1985); In re Marsosi, 218 USPQ 289, 292-293 (CAFC 1983); In re Brown, 173 USPQ 685 (CCPA 1972).

Since the Office does not have the facilities for examining and comparing applicant's vaccine with the vaccine of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the vaccine of the prior art does not possess the same material structural and functional characteristics of the claimed vaccine). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

8. Claims 107-122, 124 and 128-129 are rejected under 35 U.S.C. 102(e) as anticipated by Probst et al *(U.S. Patent No. 6,432,916, published August 13, 2002).*

Claims 107-122, 124 and 128-129 are drawn to a vaccine comprising an isolated recombinant putative membrane protein E (PMPE) polypeptide of a *Chlamydia* spp. comprising an amino acid sequence at least 90% identical to SEQ ID NO: 2 when % identity is determined using XBLAST program, score+50, word=3.

Probst et al teach pharmaceutical compositions and vaccines comprising Chlamydial polypeptides (see the Abstract). Probst et al teach that the vaccines of the invention may comprise one or more polypeptide and an immunostimulant (column 27).

Probst et al teach that any variety of immunostimulants may be employed in the vaccine compositions of the invention and an adjuvant may be included (column 27). Probst et al teach that the vaccine may include on or more immunostimulants (column 30). Probst et al teach that any vaccine provided in the invention may include a combination of antigen, immune response enhancer and a suitable carrier or excipient (column 27). Probst et al teach that vaccines of the invention may also contain other *Chlamydia* antigens either incorporated into a combination polypeptide or present within a separate polypeptide (column 27). Probst et al teach SEQ ID NO:177 which is the predicted full-length amino acid sequence for *C. trachomatis* (column 10). Probst et al teach a polypeptide (SEQ ID NO: 177) that is 98% identical to SEQ ID NO:2 and comprises the claimed peptide fragment of SEQ ID NO: 5. See enclosed sequence alignment.

Although the reference appears to disclose vaccines comprising the same purified polypeptides claimed by the applicant's, the reference does not disclose that the purified polypeptides produced by the same claimed process. However, the purification or production of protein by a particular process does not impart novelty or unobviousness to a protein when the same protein is taught by the prior art. This is particularly true when the properties of the protein are not changed by the process in an unexpected manner. See In re Thorpe, 227 USPQ 964 (CAFC 1985); In re Marsosi, 218 USPQ 289, 292-293 (CAFC 1983); In re Brown, 173 USPQ 685 (CCPA 1972).

Since the Office does not have the facilities for examining and comparing applicant's vaccine with the vaccine of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of

the prior art (i.e., that the vaccine of the prior art does not possess the same material structural and functional characteristics of the claimed vaccine). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 125-127 are rejected under 35 U.S.C. 103(a) as unpatentable over Probst *(U.S. Patent No. 6,432,916, published August 13, 2002) as applied to claims* 107-122, 124 and 128-129 above and in further view of Murdin et al *(Infection and Immunity, October 1993, p. 4406-4414).*

Claims 125-127 are drawn to a vaccine of claim 124 wherein the one or more immunogens are a DPT vaccine, a HWMP *of Chlamydia trachomatis*, or an entire organism or subunit therefrom of *Chlamydia, Neisseria* gonorrhea, HIV, *Haemophilus influenzae, Moraxella catarrhalis*, human papilloma virus, Herpes simplex virus, *Haemophilus ducreyi, Treponema palladium, Candida albicans* or *Streptococcus pneumoniae.*

Probst et al teach pharmaceutical compositions and vaccines comprising Chlamydial polypeptides (see the Abstract). Probst et al teach that the vaccines of the invention may comprise one or more polypeptide and an immunostimulant (column 27). Probst et al teach that any variety of immunostimulants may be employed in the vaccine compositions of the invention and an adjuvant may be included (column 27). Probst et al teach that the vaccine may include on or more immunostimulants (column 30). Probst et al teach that any vaccine provided in the invention may include a combination of antigen, immune response enhancer and a suitable carrier or excipient (column 27). Probst et al teach that vaccines of the invention may also contain other *Chlamydia* antigens either incorporated into a combination polypeptide or present within a separate polypeptide (column 27). Probst et al teach SEQ ID NO :177 which is the predicted full-length amino acid sequence for *C. trachomatis* (column 10). Probst et al teach a polypeptide (SEQ ID NO: 177) that is 98% identical to SEQ ID NO:2 and comprises the claimed peptide fragment of SEQ ID NO: 5. See enclosed sequence alignment.

Probst et al do not specifically teach the use of high molecular weight proteins *Chlamydia trachomatis*.

Murdin et al teach an attenuated poliovirus hybrid expressing a neutralization epitope from the major outer membrane protein of *Chlamydia trachomatis* as well as a 40kDa (high molecular weight) outer membrane protein of *Chlamydia trachomatis* (page 4406, column 2, paragraph 2), in an analogous art for the purpose of inducing a strong mucosal immune response in primates and humans (see the Abstract).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to add the poliovirus-chlamydia hybrid as taught by Murdin et al to the vaccine composition of Probst et al because Probst et al teach that vaccines of the invention may also contain other *Chlamydia* antigens either incorporated into a combination polypeptide or present within a separate polypeptide (column 27). Therefore, it would have been expected barring evidence to the contrary, that the addition of poliovirus-chlamydia hybrids to the vaccine composition of Probst et al would allow for a powerful subunit vaccine because Murdin et al teach that poliovirus infection induces a strong mucosal immune response in primates and humans which indicate that poliovirus-chlamydia hybrids could become a powerful tool for the development of chlamydial vaccines (see the Abstract).

Status of Claims

10. Claims 94-95, 99-103 and 105-106 are allowed.

Conclusion

11. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308–0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (703) 872-9306.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (571) 272-0857. The examiner can normally be reached on Monday – Friday from 9:00 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (571) 272-0864.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov./>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Vanessa L. Ford
Biotechnology Patent Examiner
August 17, 2005

NITA MINNIFIELD
PRIMARY EXAMINER
8/22/05

mail w/office action

Chlamydia trachomatis.

WO9928475-A2.

Griffais R;

Query Match 99.2%; Score 5047; DB 20; Length 989;
Best Local Similarity 99.3%; Pred. No. 0;
Matches 958; Conservative 4; Mismatches 3; Indels 0; Gaps 0;

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Qy          1 MKKAPFFFFLIGNSLSGLAREVPSRIFLMPNSVPDPTKESLSNKISLTGDTHNLTNCYLDN 60
              ||||||||||:||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         25 MKKAPFFFFLIGSSLSGLAREVPSRIFLMPNSVPDPTKESLSNKISLTGDTHNLTNCYLDN 84

Qy         61 LRYILAILQKTPNEGAAVTITDYLSFFDTQKEGIYFAKNLTPESGGAIGYASPNSPTVEI 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         85 LRYILAILQKTPNEGAAVTITDYLSFFDTQKEGIYFAKNLTPESGGAIGYASPNSPTVEI 144

Qy        121 RDTIGPVIFENNTCCRPFTSSNPNAAVNKIREGGAIHAQNLYINHNHDVVGFMKNFSYVR 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        145 RDTIGPVIFENNTCCRPFTSSNPNAAVNKIREGGAIHAQNLYINHNHDVVGFMKNFSYVR 204

Qy        181 GGAISTANTFVVSENQSCFLFMDNICIQTNTAGKGGAIYAGTSNSFESNNCDLFFINNAC 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        205 GGAISTANTFVVSENQSCFLFMDNICIQTNTAGKGGAIYAGTSNSFESNNCDLFFINNAC 264

Qy        241 CAGGAIFSPICSLTGNRGNIVFYNNRCFKNVETASSEASDGGAIKVTTRLDVTGNRGRIF 300
              ||||||||||||||||||||||||||||||||||||:|||||||||||||||||||||||||
Db        265 CAGGAIFSPICSLTGNRGNIVFYNNRCFKNVETASSESSDGGAIKVTTRLDVTGNRGRIF 324

Qy        301 FSDNITKNYGGAIYAPVVTLVDNGPTYFINNIANNKGGAIYIDGTSNSKISADRHAIIFN 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        325 FSDNITKNYGGAIYAPVVTLVDNGPTYFINNIANNKGGAIYIDGTSNSKISADRHAIIFN 384

Qy        361 ENIVTNVTNANGTSTSANPPRRNAITVASSSGEILLGAGSSQNLIFYDPIEVSNAGVSVS 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        385 ENIVTNVTNANGTSTSANPPRRNAITVASSSGEILLGAGSSQNLIFYDPIEVSNAGVSVS 444

Qy        421 FNKEADQTGSVVFSGATVNSADFHQRNLQTKTPAPLTLSNGFLCIEDHAQLTVNRFTQTG 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        445 FNKEADQTGSVVFSGATVNSADFHQRNLQTKTPAPLTLSNGFLCIEDHAQLTVNRFTQTG 504

Qy        481 GVVSLGNGAVLSCYKNGAGNSASNASITLKHIGLNLSSILKSGAEIPLLWVEPTNNSNNY 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        505 GVVSLGNGAVLSCYKNGAGNSASNASITLKHIGLNLSSILKSGAEIPLLWVEPTNNSNNY 564

Qy        541 TADTAATFSLSDVKLSLIDDYGNSPYESTDLTHALSSQPMLSISEASDNQLRSDDMDFSG 600
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        565 TADTAATFSLSDVKLSLIDDYGNSPYESTDLTHALSSQPMLSISEASDNQLRSDDMDFSG 624

Qy        601 LNVPHYGWQGLWTWGWAKTQDPEPASSATITDPQKANRFHRTLLLTWLPAGYVPSPKHRS 660
              ||||||||||||:|||||||||||||||||||||:||||||||||||||||||||||||||
Db        625 LNVPHYGWQGLWSWGWAKTQDPEPASSATITDPKKANRFHRTLLLTWLPAGYVPSPKHRS 684

Qy        661 PLIANTLWGNMLLATESLKNSAELTPSDHPFWGITGGGLGMMVYQDPRENHPGFHMRSSG 720
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        685 PLIANTLWGNMLLATESLKNSAELTPSDHPFWGITGGGLGMMVYQDPRENHPGFHMRSSG 744

Qy        721 YSAGMIAGQTHTFSLKFSQTYTKLNERYAKNNVSSKNYSCQGEMLFSLQEGFLLTKLVGL 780
              |||||||||||||||||||||||||||||||||||||||||||||||||||| |||||
Db        745 YSAGMIAGQTHTFSLKFSQTYTKLNERYAKNNVSSKNYSCQGEMLFSLQEGFLLAKLVGL 804

Qy        781 YSYGDHNCHHFYTQGENLTSQGTFRSQTMGGAVFFDLPMKPFGSTHILTAPFLGALGIYS 840
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        805 YSYGDHNCHHFYTQGENLTSQGTFRSQTMGGAVFFDLPMKPFGSTHILTAPFLGALGIYS 864

Qy        841 SLSHFTEVGAYPRSFSTKTPLINVLVPIGVKGSFMNATQRPQAWTVELAYQPVLYRQEPG 900
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        865 SLSHFTEVGAYPRSFSTKTPLINVLVPIGVKGSFMNATQRPQAWTVELAYQPVLYRQELE 924

Qy        901 IATQLLASKGIWFGSGSPSSRHAMSYKISQQTQPLSWLTLHFQYHGFYSSSTFCNYLNGE 960
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        925 IATQLLASKGIWFGSGSPSSRHAMSYKISQQTQPLSWLTLHFQYHGFYSSSTFCNYLNGE 984

Qy        961 IALRF 965
              |||||
Db        985 IALRF 989
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mail w/office action

Probst P, Bhatia A, Skeiky YAW, Fling SP, Jen S, Stromberg EJ;

Query Match 98.2%; Score 4994.5; DB 21; Length 964;
Best Local Similarity 98.4%; Pred. No. 0;
Matches 950; Conservative 7; Mismatches 7; Indels 1; Gaps 1;

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Qy          1 MKKAFFFFLIGNSLSGLAREVPSRIFLMPNSVPDPTKESLSNKISLTGDTHNLTNCYLDN 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MKKAFFFFLIGNSLSGLAREVPSRIFLMPNSVPDPTKESLSNKISLTGDTHNLTNCYLDN 60

Qy         61 LRYILAILQKTPNEGAAVTITDYLSFFDTQKEGIYFAKNLTPESGGAIGYASPNSPTVEI 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 LRYILAILQKTPNEGAAVTITDYLSFFDTQKEGIYFAKNLTPESGGAIGYASPNSPTVEI 120

Qy        121 RDTIGPVIFENNTCCRPFTSSNPNAAVNKIREGGAIHAQNLYINHNHDVVGFMKNPSYVR 180
              |||||||||||||||  ||  || ||:|||||||||||||||||||||||||||||||:
Db        121 RDTIGPVIFENNTCCRLFTWRNPYAA-DKIREGGAIHAQNLYINHNHDVVGFMKNPSYVQ 179

Qy        181 GGAISTANTFVVSENQSCFLFMDNICIQTNTAGKGGAIYAGTSNSFESNNCDLFFINNAC 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        180 GGAISTANTFVVSENQSCFLFMDNICIQTNTAGKGGAIYAGTSNSFESNNCDLFFINNAC 239

Qy        241 CAGGAIFSPICSLTGNRGNIVFYNNRCFKNVETASSEASDGGAIKVTTRLDVTGNRGRIF 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        240 CAGGAIFSPICSLTGNRGNIVFYNNRCFKNVETASSEASDGGAIKVTTRLDVTGNRGRIF 299

Qy        301 FSDNITKNYGGAIYAPVVTLVDNGPTYFINNIANNKGGAIYIDGTSNSKISADRHAIIFN 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        300 FSDNITKNYGGAIYAPVVTLVDNGPTYFINNIANNKGGAIYIDGTSNSKISADRHAIIFN 359

Qy        361 ENIVTNVTNANGTSTSANPPRRNAITVASSSGEILLGAGSSQNLIFYDPIEVSNAGVSVS 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        360 ENIVTNVTNANGTSTSANPPRRNAITVASSSGEILLGAGSSQNLIFYDPIEVSNAGVSVS 419

Qy        421 FNKEADQTGSVVFSGATVNSADFHQRNLQTKTPAPLTLSNGFLCIEDHAQLTVNRFTQTG 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        420 FNKEADQTGSVVFSGATVNSADFHQRNLQTKTPAPLTLSNGFLCIEDHAQLTVNRFTQTG 479

Qy        481 GVVSLGNGAVLSCYKNGAGNSASNASITLKHIGLNLSSILKSGAEIPLLWVEPTNNSNNY 540
              |||||||||||||||| |:|||||||||||||||||||||||||||||||||||||||||
Db        480 GVVSLGNGAVLSCYKNGTGDSASNASITLKHIGLNLSSILKSGAEIPLLWVEPTNNSNNY 539

Qy        541 TADTAATFSLSDVKLSLIDDYGNSPYESTDLTHALSSQPMLSISEASDNQLRSDDMDFSG 600
              ||||||||||||||||||||||||||||||||||||||||||||||||||||:|:::|||||
Db        540 TADTAATFSLSDVKLSLIDDYGNSPYESTDLTHALSSQPMLSISEASDNQLQSENIDFSG 599

Qy        601 LNVPHYGWQGLWTWGWAKTQDPEPASSATITDPQKANRFHRTLLLTWLPAGYVPSPKHRS 660
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        600 LNVPHYGWQGLWTWGWAKTQDPEPASSATITDPQKANRFHRTLLLTWLPAGYVPSPKHRS 659

Qy        661 PLIANTLWGNMLLATESLKNSAELTPSDHPFWGITGGGLGMMVYQDPRENHPGFHMRSSG 720
              |||||||||||||||||||||||| ||||||||||||||||||||||||||||||||||||
Db        660 PLIANTLWGNMLLATESLKNSAELTPSGHPFWGITGGGLGMMVYQDPRENHPGFHMRSSG 719

Qy        721 YSAGMIAGQTHTFSLKFSQTYTKLNERYAKNNVSSKNYSCQGEMLFSLQEGFLLTKLVGL 780
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        720 YSAGMIAGQTHTFSLKFSQTYTKLNERYAKNNVSSKNYSCQGEMLFSLQEGFLLTKLVGL 779

Qy        781 YSYGDHNCHHFYTQGENLTSQGTFRSQTMGGAVFFDLPMKPFGSTHILTAPFLGALGIYS 840
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        780 YSYGDHNCHHFYTQGENLTSQGTFRSQTMGGAVFFDLPMKPFGSTHILTAPFLGALGIYS 839

Qy        841 SLSHFTEVGAYPRSFSTKTPLINVLVPIGVKGSFMNATQRPQAWTVELAYQPVLYRQEPG 900
              |||||||||||||||||||||||||||||||||||||||| ||||||||||||||||||||
Db        840 SLSHFTEVGAYPRSFSTKTPLINVLVPIGVKGSFMNATHRPQAWTVELAYQPVLYRQEPG 899

Qy        901 IATQLLASKGIWFGSGSPSSRHAMSYKISQQTQPLSWLTLHFQYHGFYSSSTFCNYLNGE 960
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        900 IATQLLASKGIWFGSGSPSSRHAMSYKISQQTQPLSWLTLHFQYHGFYSSSTFCNYLNGE 959

Qy        961 IALRF 965
              |||||
Db        960 IALRF 964
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